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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/478,621	01/05/2000	Stephen E. Epstein	674522-2001	1917
20999	7590	05/13/2005	EXAMINER	
FROMMERM LAWRENCE & HAUG 745 FIFTH AVENUE- 10TH FL. NEW YORK, NY 10151			JIANG, DONG	
		ART UNIT		PAPER NUMBER
				1646

DATE MAILED: 05/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.	09/478,621	Applicant(s) EPSTEIN ET AL.
Examiner Dong Jiang	Art Unit 1646	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 23 March 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1.  The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
  - a)  The period for reply expires 5 months from the mailing date of the final rejection.
  - b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2.  The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3.  The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
  - (a)  They raise new issues that would require further consideration and/or search (see NOTE below);
  - (b)  They raise the issue of new matter (see NOTE below);
  - (c)  They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d)  They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4.  The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5.  Applicant's reply has overcome the following rejection(s): the rejection of claim 22 under 35 U.S.C. 112, second paragraph.
6.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7.  For purposes of appeal, the proposed amendment(s): a)  will not be entered, or b)  will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 22.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8.  The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9.  The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10.  The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11.  The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.
12.  Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_
13.  Other: \_\_\_\_\_.



Continuation of 11. does NOT place the application in condition for allowance because:

With respect to applicants request for withdrawal of finality, applicants argue that the amendment made to claim 22 in the last response simply include adding "following balloon angioplasty" and rewriting the claim in independent form, that the indefiniteness rejection is a new rejection that was not previously raised and that was not necessitated by applicants amendment. This argument is not persuasive because in addition to the amendment above as indicated by applicants, the claim also recited a new limitation of "reducing risk of restenosis", which is distinct from the original "reducing restenosis". While it is relative clear what it is meant by "reducing restenosis", it is unclear what it is meant by "reducing risk of restenosis", and how to achieve such (set forth in the preamble), i.e., how to determine the amount of VEGF-R and ang1 to be used, and what is the endpoint to be achieved. As such, the newly amended claim was indefinite, and necessitated the new ground of rejection under 35 U.S.C. 1 12, second paragraph.

With respect to the rejection of claim 22 under 35 U.S.C. 112, first paragraph, the claim remains rejected for the reasons of record set forth in the previous Office Action mailed on 17 May 2004, and 03 November 2004. Applicants argue that the art by Nambu et al. (Gene Therapy, 2004, 11:865-873) examined ocular neovascularization, which is a model relevant to restenosis, and demonstrates that the overexpression of Ang1 and reduction of VEGF expression reduce neovascularization in these models, which results exactly parallel the disclosure of the present application. Applicants argument has been fully considered, but is not deemed persuasive for the following reasons: first, the Nambu reference never indicates that ocular neovascularization model is a model relevant to restenosis (the present invention). Second, Nambu teaches that the effect of Ang1 may vary depending upon the setting as it is proangiogenic agent when increased expression in skin, and double transgenic mice with coexpression of Ang1 and VEGF had an additive effect on angiogenesis (page 866, the left column). Therefore, it is extremely unpredictable as to the action of Ang1 on angiogenesis. The present specification provides no actual experimental evidence relevant to the claimed invention. Thus, undue experimentation would be required of the skilled artisan to use the claimed invention.



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